

BEST AVAILABLE COPY

RECEIVED
CENTRAL FAX CENTER
SEP 26 2006Please type a plus sign (+) inside this box → ☐PTO/SB/21 (08-00)
Approved for use through 10/31/2002. OMB 0851-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

TRANSMITTAL FORM (to be used for all correspondence after initial filing)	Application Number	10/516,500
	Filing Date	29 Nov 04
	First Named Inventor	H.L. HANCKE
	Group Art Unit	1625
	Examiner Name	N. RAHMANI
Total Number of Pages In This Submission	Attorney Docket Number	HP Ingrad.

ENCLOSURES (check all that apply)		
<input type="checkbox"/> Fee Transmittal Form	<input type="checkbox"/> Assignment Papers (for an Application)	<input type="checkbox"/> After Allowance Communication to Group
<input type="checkbox"/> Fee Attached	<input type="checkbox"/> Drawing(s)	<input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences
<input type="checkbox"/> Amendment / Reply	<input type="checkbox"/> Licensing-related Papers	<input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief)
<input type="checkbox"/> After Final	<input type="checkbox"/> Petition	<input type="checkbox"/> Proprietary Information
<input checked="" type="checkbox"/> Affidavits/declaration(s)	<input type="checkbox"/> Petition to Convert to a Provisional Application	<input type="checkbox"/> Status Letter
<input type="checkbox"/> Extension of Time Request	<input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address	<input type="checkbox"/> Other Enclosure(s) (please identify below):
<input type="checkbox"/> Express Abandonment Request	<input type="checkbox"/> Terminal Disclaimer	
<input type="checkbox"/> Information Disclosure Statement	<input type="checkbox"/> Request for Refund	
<input type="checkbox"/> Certified Copy of Priority Document(s)	<input type="checkbox"/> CD, Number of CD(s) _____	
<input type="checkbox"/> Response to Missing Parts/ Incomplete Application	Remarks	
<input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT	
Firm or Individual name	Mark Pohl, Esq., USPTO Reg. No. 35,325 Pharmaceutical Patent Attorneys, LLC 55 Madison Avenue, 4th floor, Morristown, NJ 07960-7397 USA
Signature	/s/
Date	see below date

CERTIFICATE OF MAILING	
I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231 on this date: <input type="text" value="see below date"/>	
Typed or printed name	
Signature	Date 26 Sept 06

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

RECEIVED
CENTRAL FAX CENTER

SEP 26 2006

PTO/SB/97 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Certificate of Transmission under 37 CFR 1.8

I hereby certify that this correspondence is being facsimile transmitted to the
United States Patent and Trademark Office Central Fax Center
(571)273-8300

on 26 Sept 06
Date

Mark Pohl

Signature

J. Mark Pohl, Reg. No. 35,325

Typed or printed name of person signing Certificate

Note: Each paper must have its own certificate of transmission, or this certificate must identify
each submitted paper.

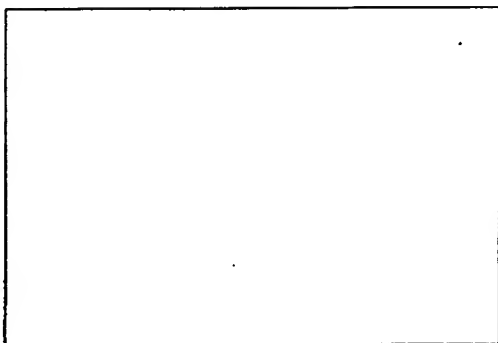
The submitted papers are enumerated on the enclosed Transmittal Form,
PTO Form SB/21.

Burden Hour Statement: This form is estimated to take 0.03 hours to complete. Time will vary depending upon the needs of the individual case.
Any comments on the amount of time required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark
Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents,
Washington, DC 20231.

RECEIVED
CENTRAL FAX CENTER
SEP 26 2006

In The United States Patent Office

5



Serial No. : 10/516,500
Filing Date: 29 November 2004
Group Art: 1625
Examiner: Niloofar RAHMANI, Esq.

RULE 132 DECLARATION

20

I am an inventor of record of the captioned application. I present this Declaration pursuant to The Code of Federal Regulations, Title 37, Rule 132. I hereby Declare as follows:

25

1. I have read the Examiner's 1 August 2006 Office Action and the references cited therein. I respectfully disagree with certain of the factual allegations made by the Examiner because the art of record contradicts the Examiner.
2. The Examiner alleges, "*Andrographis paniculata* grown just anywhere everywhere on this planet may or my [sic] not have the compounds necessary to treat Syndrome X." I respectfully disagree, for several reasons.

Juan Luis HANCKE OROZCO *et al.*

Serial No. 10/516,500

Priority Date: 03 February 2004

Diterpenic Labdanes . . .

3. First, *Andrographis paniculata* cannot, to my knowledge, grown "anywhere everywhere on this planet." To the contrary, like any other plant, it has specific environmental conditions for growth; these conditions are well known in the art, and well known to any botanist familiar with the plant.

5 4. Second, I have no reason to believe that "*Andrographis paniculata* ... may or my [*sic*] not have the compounds necessary to treat Syndrome X." To the contrary, every specimen of *Andrographis paniculata* which I have evaluated, from whatever source or ecosystem, has in fact contained "the compounds necessary to treat Syndrome X." I therefore know of no factual
10 evidence to support the thesis that *Andrographis paniculata* from a certain specific ecosystem "may or my [*sic*] not have the compounds necessary to treat Syndrome X."

5. Our application claim number 53 reads as follows:

53. A method comprising:

- 15 i. diagnosing in a patient a disease selected from the group consisting of: Alzheimer's Disease; Acquired Immune Deficiency Syndrome; and autoimmune disease, and
20 ii. administering to said patient 3-[2-[decahydro-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-2-methylene-1-naphthalenyl]ethylidene]-dihydro-4-hydroxy-2(3h)-furanone in an amount effective to combat said disease.

I understand that "It is the examiner's position that the claims are drawn to 'a method of diagnosing in a patient a disease.'" I respectfully disagree because the

DECLARATION - Page 2

Juan Luis HANCKE OROZCO *et al.*
Serial No. 10/516,500
Priority Date: 03 February 2004
Diterpenic Labdanes . . .

Examiner's position ignores the entire second half of our claim. Contrary to the Examiner's position, one of skill in the art would read this two-step claim to be drawn not to a one-step method (diagnosing), but to a two-step method requiring both i) diagnosing and ii) administering.

5 6. I understand the Examiner to allege that the meaning of the term
"Andrographolide" is well-known in the art and denotes one specific
compound. I respectfully disagree. The Examiner's own references show that
this term is used by different scientists to denote different compounds. For
example, the Examiner notes that U.S. Patent No. 5,883,074 uses the term to
10 denote one compound, while US Patent Application 2002/0077350 and US
2002/0068098) use the same term to denote a different compound.

15 7. I understand the Examiner to allege that the compound allegedly known as
"andrographolide" is the same as the claimed compound. As support, the
Examiner at page 3 of her Office Action illustrates the compound which she
understands to be the same as the claimed compound. I respectfully disagree
that the Examiner's compound is the same as – nor even similar to – the
claimed compound. Rather, the structural differences between the Examiner's
compound and the claimed compound are readily apparent when one
compares the two chemical structures. I illustrate the differences here,

DECLARATION - Page 3

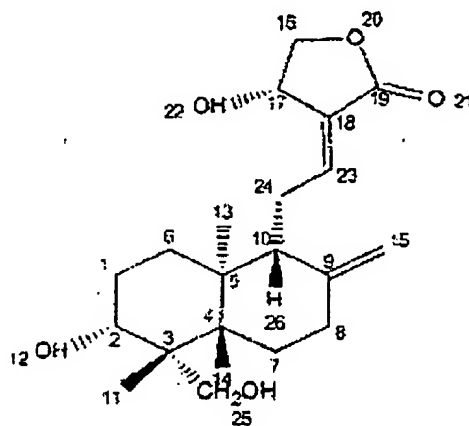
Juan Luis HANCKE OROZCO *et al.*

Serial No. 10/516,500

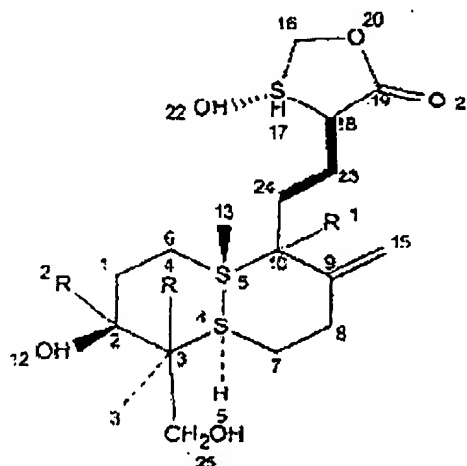
Priority Date: 03 February 2004

Diterpenic Labdanes . . .

showing the structure of the claimed compound on the top, and the structure of the Examiner's compound on the bottom. One of skill in the art would, on seeing these two different structures, immediately apprehend that the compounds are not the same, and may indeed possess widely different pharmaceutical and toxicology profiles.



8. As a related matter, the Examiner at pages 3-4 provides the incorrect IUPAC nomenclature designation for her compound. While a precise IUPAC designation is not possible (the Examiner's compound bears a number of substituted R moieties), the



The Examiner's compound

Examiner's compound includes three sulfur atoms. The IUPAC name she provides, however, makes no mention of any of these.

DECLARATION - Page 4

Juan Luis HANCKE OROZCO *et al.*

Serial No. 10/516,500

Priority Date: 03 February 2004

Diterpenic Labdanes . . .

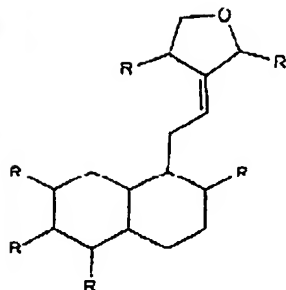
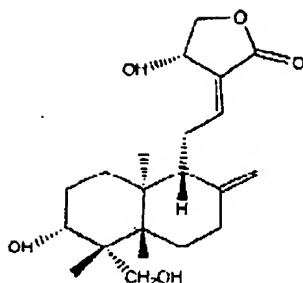
- 5 9. I further note that the art of record fails to teach the claimed compound. The prior art teaches "andrographolide." See e.g., BABISH *et al.*, U.S. '098. Our claims, however, do not require "andrographolide"; rather, our claims require 3-[2-[decahydro-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-2-methylene-1-naphthalenyl]ethylidene]-dihydro-4-hydroxy-2(3h)-furanone. This compound is not taught by the art of record. This is illustrated in the accompanying comparison of the claimed compound and the five compounds taught by the art of record.

DECLARATION - Page 5

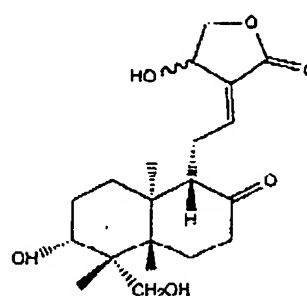
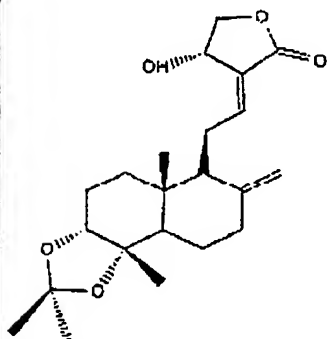
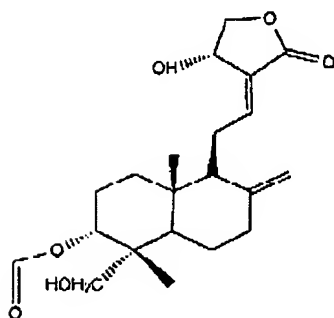
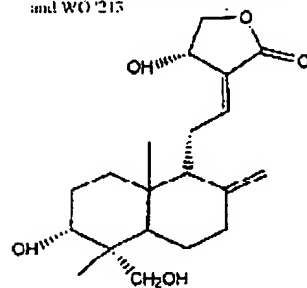
Juan Luis HANCKE OROZCO *et al.*

Serial No. 10/516,500

Priority Date: 03 February 2004

Diterpenic Labdanes ...John G. BABISH *et al.*, WO '605

The claimed compound

John G. BABISH *et al.*, U.S. '998
G.D. WHEELLOCK *et al.*, U.S. '994; U.S. '063
and WO '213NANDURI *et al.*, U.S. '324NANDURI *et al.*, U.S. '196NANDURI *et al.*, U.S. '590

For example, BABISH *et al.*, WO '605 and NANDURI *et al.*, U.S. '324, U.S. '590, and U.S. '196 (2002) fail to teach methylation at C4. Similarly, BABISH *et al.* U.S. '098, and WHEELLOCK *et al.*, U.S. '994, U.S. '063 and WO '213 fail to teach oxidation at C9. One of skill in the art would not read any of the references of record to teach nor fairly suggest the claimed compound.

10. Similarly, our claims are drawn to methods to treat AIDS, Syndrome X, non-autoimmune Alzheimer's Disease, and autoimmune disease. One of skill in the art would not read the art of record to teach these uses. For example, one

DECLARATION - Page 6

Juan Luis HANCKE OROZCO *et al.*

Serial No. 10/516,500

Priority Date: 03 February 2004

Diterpenic Labdanes . . .

of skill in the art would read BABISH *et al.*, U.S. '098 and U.S. '350, to teach the use of "andrographolide" as a diterpene triepoxide lactone or triptolide adjunct. Similarly, one of skill in the art would read BOGGS *et al.*, U.S. '269 to teach the use of "andrographolide" as an antibiotic adjunct.

5 11. I respectfully disagree with the Examiner's factual assertion that "bacterial infection is broadly encompassed by AIDS" because AIDS does not encompass bacterial infection. AIDS is caused by an infection by a retrovirus, not a bacterium. The two different classes of infection require two completely different therapies. For example, AIDS is treated by anti-retroviral drugs, while bacterial infection is treated by antibiotics. Further, anti-retroviral drugs are structurally dissimilar from antibiotics. Further, no anti-viral drug has been shown effective against bacterial infection, and no antibiotic has been shown effective against AIDS.

10 12. One of skill in the art would read NANDURI *et al.*, U.S. '196, to teach that "andrographolide"-containing preparations "have been assayed for the ability to decrease the expression and phosphorylation of p34^{cdc2} kinase, cyclin B and c-Moss for treating or preventing pathogenicity." One of skill in the art would read NANDURI '196, however, to fail to teach *the results* of those assays (that is, he fails to say whether or not the assays show any effect). One of skill in

DECLARATION - Page 7

Juan Luis HANCKE OROZCO *et al.*

Serial No. 10/516,500

Priority Date: 03 February 2004

Diterpenic Labdanes . . .

the art would read NANDURI '196 to therefore provide a mere "invitation to experiment," not an enabling prior art disclosure of the claimed uses.

13. One of skill in the art would read PANOSSIAN *et al.*, to teach the use of "andrographolide" for "*in vitro* effect on the activation and proliferation of immunocompetent cells." In contrast, autoimmune disease is thought to be caused by an overly-active immune system. Therefore, by teaching that andrographolide *activates* the immune system, one of skill in the art would read PANOSSIAN to teach away from the use of the claimed compound to treat autoimmune diseases.

14. One of skill in the art would read WHEELLOCK *et al.*, WO '213 to teach oncology and tumor treatment. One of skill in the art would read WHEELLOCK *et al.*, U.S. '994, to teach anal tumor treatment.

15. One of skill in the art would understand that predictability in the pharmaceutical art is low because minor structural differences can precipitate major changes in toxicology or clinical efficacy. This shows that it would not have been obvious to modify any of the prior art compounds to *make* the claimed compound, and that it would not have been obvious to *use* such a modified compound for the claimed uses.

DECLARATION - Page 8

Juan Luis HANCKE OROZCO *et al.*

Serial No. 10/516,500

Priority Date: 03 February 2004

Dierpentic Labdanes . . .

I further hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United State Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon or any patent to which this verified statement is directed.

Professor Juan Luis HANCKE OROZCO, Ph.D.
Dated as of 9 September 2006

SD\HP Ingredients\10.xxx,xxx - Amendment - Preliminary.doc

DECLARATION - Page 9

13.SEP.2006 9:40

IDB HOLDING +39 2 57496290

NR.554

P.9/9

Juan Luis HANCKE OROZCO *et al.*

Serial No. 10/516,500

Priority Date: 03 February 2004

Diterpenic Lahdanes ...

I further hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United State Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon or any patent to which this verified statement is directed.



10 Professor Juan Luis HANCKE OROZCO, Ph.D.
Dated as of 9 September 2006

SDAHP Ingredients\10xxxxxxx - Amendment - Preliminary.doc

DECLARATION - Page 9

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

☐ BLACK BORDERS

☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES

☐ FADED TEXT OR DRAWING

☒ BLURRED OR ILLEGIBLE TEXT OR DRAWING

☐ SKEWED/SLANTED IMAGES

☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS

☐ GRAY SCALE DOCUMENTS

☒ LINES OR MARKS ON ORIGINAL DOCUMENT

☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY

☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.